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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,758	02/27/2004	Joseph Cohen	B45187 C1	1891

7590 12/08/2006

GLAXOSMITHKLINE
Corporate Intellectual Property - UW2220
P.O. Box 1539
King of Prussia, PA 19406-0939

EXAMINER	
MINNIFIELD, NITA M	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 12/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/789,758	**Applicant(s)** COHEN ET AL.	
	Examiner N. M. Minnifield	**Art Unit** 1645	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 25 October 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *4* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *10/25/06*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *13 16-22*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☒ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). 10/25/06
13. ☐ Other: _____.

N. M. Minnifield
Primary Examiner
Art Unit: 1645

ADVISORY ACTION

1. Applicants' amendment filed October 25, 2006 is acknowledged and has been entered. Claims 13 and 16-22 are now pending in the present application. All rejections have been withdrawn in view of Applicants' amendment to the claims and/or comments, with the exception of those discussed below.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 13 and 16-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stoute et al (New England J. Medicine, January, 1997, 336:89-91) taken with Davis et al 6406705.

Claims 13 and 17-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stoute et al (New England J. Medicine, January, 1997, 336:89-91) taken with Krieg et al 6207646

Claims 13, 17-19 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stoute et al (New England J. Medicine, January, 1997, 336:89-91) taken with Raz et al 6579940

4. The 103 obviousness rejections as set forth above have been maintained for the reasons as set forth in the Final Rejection mailed June 23, 2006. Applicant's arguments filed October 25, 2006 have been fully considered but they are not

persuasive. Applicants have asserted that there is no suggestion and/or motivation in Stoute et al to combine the prior art (Davis; Krieg et al; Raz et al). However, the combination of references taken as a whole teaches the claimed composition (antigen and CpG oligonucleotide) for raising an immune response as well as methods prevention or amelioration of plasmodium infection in a patient. With regard to Stoute et al, it is noted that Applicants are arguing the references individually. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicants have asserted that at least one of the vaccines, specifically vaccine 1, of Stoute et al had lower immune responses than vaccines 2 and 3. Applicants have asserted combining alum and MPL demonstrates a lesser effect than the other two and that there is no suggestion in Stoute et al to combine alum with any other adjuvant, particularly CpG, with a hybrid malarial antigen, as disclosed in the instant application. However, it is noted that the claims are directed to compositions that raise an immune response; the claims do not set a limitation on the degree of the immune responses. Even if a reference discloses an inoperative device, it is prior art for all that it teaches." Beckman Instruments v. LKB Produkter AB, 892 F.2d 1547, 1551, 13 USPQ2d 1301, 1304 (Fed. Cir. 1989). Therefore, "a non-enabling reference may qualify as prior art for the purpose of determining obviousness under 35 U.S.C. 103." Symbol Techs. Inc. v. Opticon Inc., 935 F.2d 1569, 1578, 19 USPQ2d 1241, 1247 (Fed. Cir. 1991). A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. W.L. Gore &

Associates, Inc. v. Garlock, Inc., 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984) The prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed...." In re Fulton, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004).

Applicants have asserted that Davis, et al. is directed to combinations of CpG with non-nucleic adjuvants; Davis, et al. does not disclose advantages of CpG alone with a malarial antigen. In addition, Davis, et al. merely recite a laundry list of bacterial, viral and parasitic antigens, but do not disclose any hybrid malarial antigens. In particular, Davis, et al. do not teach the use of a hybrid antigen such as RTS,S or RTS,S* in combination with CpG adjuvant. Thus, Applicants respectfully submit that there is no teaching or suggestion in either reference, either alone or in combination, to combine hybrid malarial antigens with CpG adjuvant. Even if, arguendo, there were a suggestion to combine CpG adjuvant with hybrid malarial antigens, neither Stoute, et al. nor Davis, et al. provide any expectation of success in developing a composition for raising an immune response. In fact, Stoute, et al. teaches that the choice of adjuvant can have significant effects on immune response and protection, with certain adjuvants enhancing a greater protective response than others. Thus, the skilled artisan would not have a reasonable expectation of success developing a composition capable of eliciting an immune response to a malarial antigen simply by combining any adjuvant and any malarial antigen. The Applicants respectfully submit that the Examiner has, therefore, not met either prong of her burden under In re Vaeck. It is the Examiner's position that the combination of references (Stoute et al in view of

Davis; Stoute et al in view of Krieg et al; Stoute et al in view of Raz et al) teach the claimed compositions for raising an immune response as well as methods of prevention or amelioration of plasmodium infection in a patient. A parasitic antigen would encompass a malarial antigen. As previously stated, the combination of adjuvants can be used with an antigen to mount an antigen specific immune response that is capable of reducing the level of or eradicating the infectious pathogen. An infectious disease, as used herein, is a disease arising from the presence of a foreign microorganism in the body." (Davis, col. 8) It would have been obvious to a person of ordinary skill in the art at the time the invention was made to prepare a composition comprising the RTS,S and adjuvant (CpG or CpG and aluminum salts) since the prior art teaches that the RTS,S was a better vaccine composition when a combination of adjuvants were present. Further, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to use the CpG adjuvant in a vaccine composition for administration to a human since the art teaches that the CpG is a potent adjuvant and that it induces a Th1-type immune response, including Th1 cytokines such as IL-12 and interferon gamma for protection against various pathogens including parasites. It would have been obvious to a person of ordinary skill in the art at the time the invention was made that there would be a reasonable expectation of success of preventing or ameliorating plasmodium infection in a patient if the prepared composition taught by Stoute et al taken with Davis et al were administered to the patient.

The same is true for Stoute et al in view of Krieg et al and Stoute et al in view of Raz et al. Absent any convincing or unexpected evidence to the contrary, the claimed invention is prima facie obvious in view of the combined teachings of

the prior art. Further it is noted that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. In re Fout, 675 F.2d 297, 213 USPQ 532 (CCPA 1982).

5. No claims are allowed.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system,

contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

N. M. Minnifield
Primary Examiner
Art Unit 1645

NMM
December 5, 2006